Pharmaceutical benefit-risk perception and age differences in the USA and Germany

Benefit-Risk Perception and Age Differences in the USA and Germany

By

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Abstract

The role of older age in patients' perceptions of the benefits and risks of medical treatments has hardly been empirically investigated. This study explored benefit-risk perception age differences between adults aged 65 years old and over (older group) and those aged 18-64 years old (younger group). An online survey – representative for age, sex, and education – was conducted in Ohio, USA (N=1,520), and Germany (N=1,536). The results showed clear age differences that strongly support recent pilot findings. Older adults perceived prescription medicines – including their benefits, and effectiveness – significantly more positively than their younger counterparts. They were more likely to have significantly higher benefit and lower risk perceptions for most, but not all, medical treatments investigated. In forming these perceptions, older adults relied much more on positive/negative affect, that is, their positive/ negative experiences and feelings of "goodness" or "badness" they associated with each medicine, medical procedure, or test investigated. They also consistently perceived doctors and pharmacists as more competent and trustworthy. Contrary to popular belief, however; both age groups ranked their reliance on 15 different medical (e.g. doctors), societal (e.g. social media), and industry (e.g. pharmaceutical company websites) sources of medicines information remarkably similarly. Adults of all ages also were more likely to attribute the causes of side effects to patients over any other actor. The study concludes by emphasizing the importance of furthering our knowledge of age differences in patients' benefit-risk perceptions.

Declarations

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Availability of data and material
The survey data generated during the current study are available from the corresponding author on reasonable request.

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(1.) Introduction

Understanding how patients of all ages perceive the benefits and risks of medical treatments is vitally important. A wealth of research has demonstrated that benefit-risk perceptions can influence patients' (1) medicine-taking behaviour such as their treatment choices and regimen compliance; (2) acceptability of adverse reactions; (3) attitudes towards medical, societal, and industry actors; and (4) information-seeking behaviour such as where to obtain medicines information and which sources to trust [1-9]. Benefit-risk perception knowledge can, in turn, inform pharmacovigilance interventions and is widely recognized as a pre-requisite for designing effective benefit-risk communication programs [3, 10-12]. Communicators, such as government regulators and patient advocacy groups, can, for example, design more effective tools, which can correct patients' misconceptions, strengthen accurate beliefs, and add missing information that is "material" to decision-making [8, 13-14].

Age differences have received remarkably little attention in benefit-risk perception research [15]. The vast majority of early studies were confined to student samples or paid little attention to age. Thousands of more recent studies have either not reported age-related results or presented age as a confounder of a stronger relationship with another variable such as gender, risk beliefs, or trust [16]. Researchers have been more interested in other factors such as the characteristics of hazards (e.g. voluntariness, controllability, uncertainty), or characteristics of perceivers other than age (e.g. gender, race, nationality) [17-20]. While some medical studies have used older samples to examine adults' benefit-risk perceptions, e.g. [21-22], far fewer have specifically investigated differences (and similarities) *between* older and younger adults [23]. This lack of age research is particularly surprising in the medical domain considering older adults consume the highest percentage of medicines by age group and are far more likely than their younger counterparts to have multiple chronic diseases such as hypertension, heart disease, and diabetes [24-26]. Indeed, older adults face a bewildering array of benefit-risk decisions about numerous medicines, medical procedures, and tests [27].

Despite the dearth of benefit-risk perception studies, a burgeoning literature provides strong evidence that older age has a profound influence on individuals' judgements and decision-making [28-31]. For example, Mikels *et al*. [32] reviewed a raft of research identifying age-related changes in cognition, emotion, and motivation across the lifespan. Finucane [33] suggests numerous ways that such findings *might* be relevant and applicable to benefit-risk perception and communication. Yet, beyond these constructive suggestions, few applied studies have been conducted outside of financial and automotive contexts [23, 30]. One exception is a recent medical domain pilot study [15] that identified clear benefit-risk perception differences between adults aged 58-93 years old (older group), and those aged 31-50 years old (younger group). Amongst other results, older adults perceived greater risk today than 20 years ago compared to their younger counterparts and their quantitative benefit-risk judgements were influenced by the positive/ negative feelings they most associated with different medical treatments [15]. Taken together, these studies provide good reason to believe that older age has an influential effect on pharmaceutical benefit-risk perception. However, more extensive research is needed, including representative studies that can test the generalizability of recent pilot findings.

This study seeks to significantly contribute to understanding the role of older age in patients' pharmaceutical benefit-risk perceptions. The primary goal was to test the generalizability of recent pilot findings in representative populations (*see* [15]). In particular, the study explored whether older versus younger adults are more likely to (1) associate medicines to their benefits and perceive them as effective; (2) trust their doctors and pharmacists, rate them highly, and rely on them as sources of medicines information; and (3) perceive lower risks and higher benefits from different medical treatments. Following recent decision-making age research [32], the study also examined whether older compared to younger adults rely more on affective imagery when judging the benefits and risks of medical treatments.

(2.) Methods

(2.1) Sample

The data for this study originates from a representative online survey conducted from 21 March to 7 May 2019 by Qualtrics, an online panel provider[1]. A random quota sample was obtained with 3,056 respondents from the US state of Ohio (hereafter, "Ohio") (N=1,520), and Germany (N=1,536). The authors were resource-limited to surveying two geographic regions[2]. Ohio is a bellwether state, that is, a geographic region where the public's political tendencies match in microcosm those of the wider US [34]. While the entire US population of over 325 million could have been sampled, choosing a particularly representative state enabled more in-depth and reliable age comparisons. Germany was chosen as one of the largest countries in Europe with the national regulator, the German Federal Institute for Drugs and Medical Devices (BfArM[3]), playing a particularly important role in EU pharmaceutical regulation [36]

The sample was constrained to represent each population, Ohio and Germany, on distribution of sex, age, and educational attainment (Supplemental Table 1). Further information was collected on respondents' home county in Ohio and Länder in Germany, income bracket, political ideology ranging from very liberal to very conservative, and job status, as well as several questions on medical insurance (e.g. Medicare eligibility in Ohio).

Age group	Ohio sample %	Ohio population %	Germany sample %	Germany population %
18-24 years	10	10	8	8
25-34 years	12	14	14	14
35-44 years	14	13	14	13
45-54 years	14	15	14	17
55-64 years	16	15	17	15
65-74 years	26	17	16	17
75+ years	8	16	17	16

(2.2) Questionnaire

[1] The study was approved by King College London's Research Ethics Office (MRA-18/19-10710).
[2] It is hoped that future studies can test this study's results in other geographic regions.
[3] In German: Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM).

An online questionnaire was modelled on survey instruments created by Balog-Way and Löfstedt [15] and Paul Slovic and colleagues [1-3]. Respondents took a median of 18 minutes to complete the survey.

Part 1: Associations to prescription medicines. Respondents were shown the words 'Prescription Medicines' three times. Each time they were asked to type the first thought or association that came to mind. They then indicated whether each association was negative, neutral, or positive. The so-called 'continued associations' technique is a "sensitive indicator of the imagery and meaning associated with people's mental representations for a wide variety of concepts" (p82 [3]) and has been used in previous pharmaceutical benefit-risk perception studies (e.g. 15).

Part 2: Sources of medicines information. Three questions were asked about various sources of prescription medicines information in order to investigate respondents':

1. Perceptions of doctors, pharmacists, regulatory authorities, pharmaceutical companies, and patients in making sure medicines are safe and effective;
2. Trustworthiness of the same sources in providing advice on medicines; and
3. Reliance on obtaining information on prescription medicines from medical (e.g. doctors, pharmacists), societal (e.g. patient advocacy groups, family and friends, social media), and industry (e.g. pharmaceutical companies) information sources[4].

Part 3: Effectiveness and side effects perceptions. Respondents were asked how often they believe (1) medicines work as intended for patients, and (2) patients experience unwanted effects/ side effects from medicines. They were then presented with a list of seven possible causes of side effects and asked how often they think each one is the cause. Each one related to either patients (e.g. the patient had insufficient information), the domestic healthcare system (e.g. the patient's health plan restricted access to safer medicines), or the role of government regulators, doctors, or pharmacists.

Part 4: Risk and benefit perceptions. Respondents were asked to rate the risks and then benefits of 18 medical treatments on a scale from 1 to 7 (Table 1). The questions can be categorized as *general* measures of benefit and risk perception (*see* Wilson *et al*. 2019). "Risk" and "benefit" were intentionally not defined, and respondents were left to interpret what the terms meant to them for each medical treatment. The items were 12 prescription or over the counter medicines, 2 vaccines, 2 medical procedures, and 2 medical tests (Table 2). A variety of items were chosen, and most have been used in previous risk perception surveys.

Table 1: Risk and benefit perception questions

Risks	To what extent would you say that adults who are taking or undergoing this medical treatment are at risk of experiencing personal harm from it?' (1 = they are not at risk; 7 = they are very much at risk)
Benefits	In general, how beneficial do you consider this treatment to be? (1 = not at all beneficial; 7 = very beneficial).

Table 2: Eighteen medical treatments

Medicines to treat depression	Vitamin pills
Medicines to treat Alzheimer's Disease	Blood pressure medicines
Medicines to treat erectile dysfunction	MMR vaccine

[4] Medical, societal, and industry medicines information source categories were previously identified in multi-national surveys [9].

Antibiotics	Flu vaccine
Sleeping pills	Allergy medicines
Herbal medicines	Heart surgery
Cancer chemotherapy	Medical X-rays
Insulin	Prostate screening tests
Medicines for cholesterol (e.g. statins)	Acupuncture

Part 5: Affective imagery. One further question sought to measure the positive/ negative affect that respondents attach to the same 18 medical treatments (Table 2). 'Affect' is defined as "the experience (with or without consciousness) of "goodness" or "badness" associated with external events and objects or internal representations (e.g. memories)" [33, 36]. Research dating to at least the 1960s has consistently shown the importance of affect (and emotion) in risk and benefit perception [37]. Moreover, age research strongly suggests that older adults are particularly reliant on affective processes in decision-making [32, 38], including recent prescription medicines studies [15]. The authors therefore deliberately sought to capture affective dimensions of respondents' perceptions.

To measure affect, respondents were asked to type the first feeling that comes to mind when thinking about 18 medical treatments. They then rated each feeling on a scale from 1 (very negative) to 7 (very positive). This enabled the authors to quantitatively measure the positive/ negative affective imagery or positive/ negative feelings of 'goodness' or 'badness' that respondents associated with each medical treatment.

(2.3) Analysis

Results were analysed using SPSS. To examine age differences, two groups were defined: (1) "younger" respondents aged 18-64 years old; and (2) "older" respondents aged 65 years old and over. Although a variety of age group delineations have been used previously (Finucane, 2008; Hess *et al*. 2015), the 65+ "older" age group was chosen as it corresponds with specific socio-economic and medicines-related milestones in both the US and Germany (e.g. retirement, Medicare eligibility). The analysis predominantly relies on chi-square tests on crosstabs, independent samples t-tests, and correlations to examine differences between the two age groups.

(3.) Results

(3.1) Positive and negative affect

Respondents gave a total of 9,168 spontaneous associations to the term "Prescription Medicines". Older vs. younger adults were significantly more likely to make positive associations to the stimulus in both Ohio (+8% more older adults; 45% older vs. 37% younger) and Germany (+25%; 44% vs. 19%) ($p<0.001$ on a chi-square test in both Ohio [Phi = 0.11] and Germany [Phi = 0.17]).

Respondents were later asked to indicate the first feeling or emotion that comes to mind when thinking about 18 specific medical treatments (Table 2). A total of 42,958 spontaneous associations were made. After typing each association, a rating was provided on a scale from 1 (very negative) to 7 (very positive). The geometric mean was calculated for all treatments and ranged from 4.97 (older adults and insulin) to 2.97 (older adults and sleeping pills) (Figure 1).

Age differences were calculated by subtracting older and younger respondents' geometric mean ratings (Figure 1). Crucially, older adults were significantly more likely to make positive associations to 8/18 medical treatments ($p<0.05$ in an independent samples t-test): the flu vaccine (+0.82 difference between older vs. younger adults), heart surgery (+0.81), insulin (+0.76), antibiotics (+0.70), blood pressure medicines (+0.66), medical x-rays (+0.47), cancer chemotherapy (+0.42), and the MMR vaccine (+0.41). Older adults were only significantly more likely to rate sleeping pills less positively (-0.21 difference). No statistically significant age differences were found for the remaining 9/18 treatments.

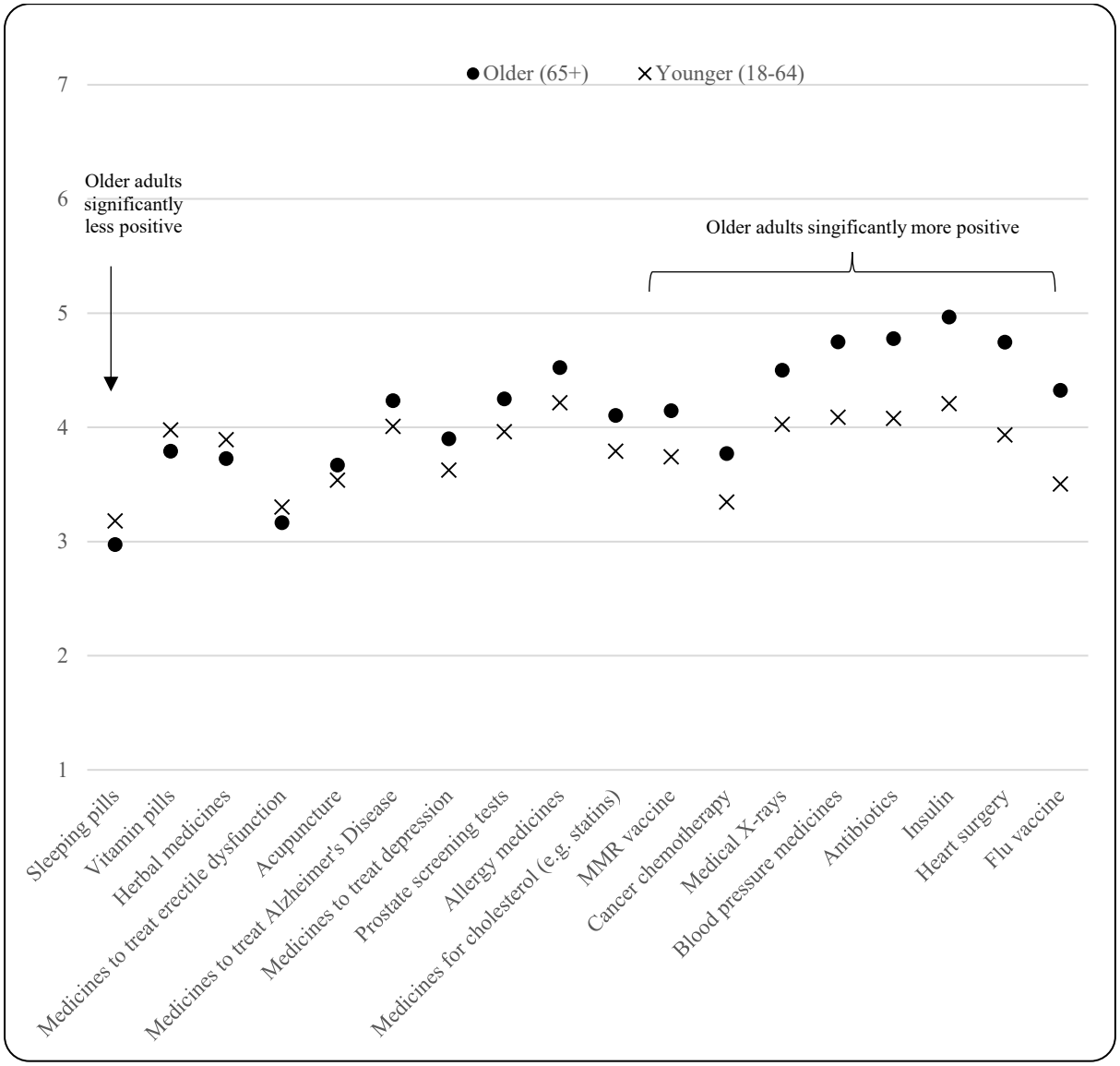

Figure 1: Geometric mean for older and younger adults positive/ negative associations to 18 medical treatments (1 = Very Negative; 7 = Very Positive).

(3.2) Medicines information sources

Respondents rated five key medical actors in making sure prescription medicines are safe and effective on a 5-point scale from excellent to poor. Prescribing doctors and pharmacists topped the list with 80% rating both as either excellent, very good, or good. Around two-thirds rated BfArM (70% of Germany population), patients taking prescription medicines

(69%), and the US Food and Drug Administration (FDA) (66% of Ohio population) as at least good. Pharmaceutical companies were rated lowest with 59% indicating they are at least good in ensuring medicines as safe and effective.

In both Germany and Ohio, older vs. younger adults were significantly more likely to rate prescribing doctors (+11% Ohio and +10% Germany more older adults) and pharmacists (+12% Ohio and +9% Germany), as at least good in ensuring that prescription medicines are safe and effective ($p<0.05$ on a chi-square test). The Phi values (effect sizes) indicated that age differences explained at least 15% of the variation in ratings of doctors and pharmacists in both regions. No significant age differences were found in both Germany and Ohio between respondents' ratings of pharmaceutical companies, the FDA, BfArM, or patients.

Respondents were then asked to rate the trustworthiness of the same information sources in providing medicines advice. At the top of the list again, doctors (3.79 mean on the five-point scale) and pharmacists (3.77) were rated as the most trustworthy sources. This was followed by patients taking prescription medicines (3.27), the FDA in Ohio (3.25), and BfArM in Germany (3.18). Out of all five actors, pharmaceutical companies (2.92) were rated as the least trustworthy source of medicines information.

Similar to respondents' ratings of actors in ensuring medicines are safe and effective, older vs. younger adults in both Ohio and Germany were significantly more likely to rate prescribing doctors (+0.14) and pharmacists (+0.11) as *more* trustworthy (Figure 2). In contrast, older adults were significantly more likely to rate pharmaceutical companies (-0.28) and especially BfArM (-0.52) as *less* trustworthy than their younger counterparts. No significant differences were found between older and younger adults' trustworthiness of 'patients taking prescription medicines' or 'the FDA'.

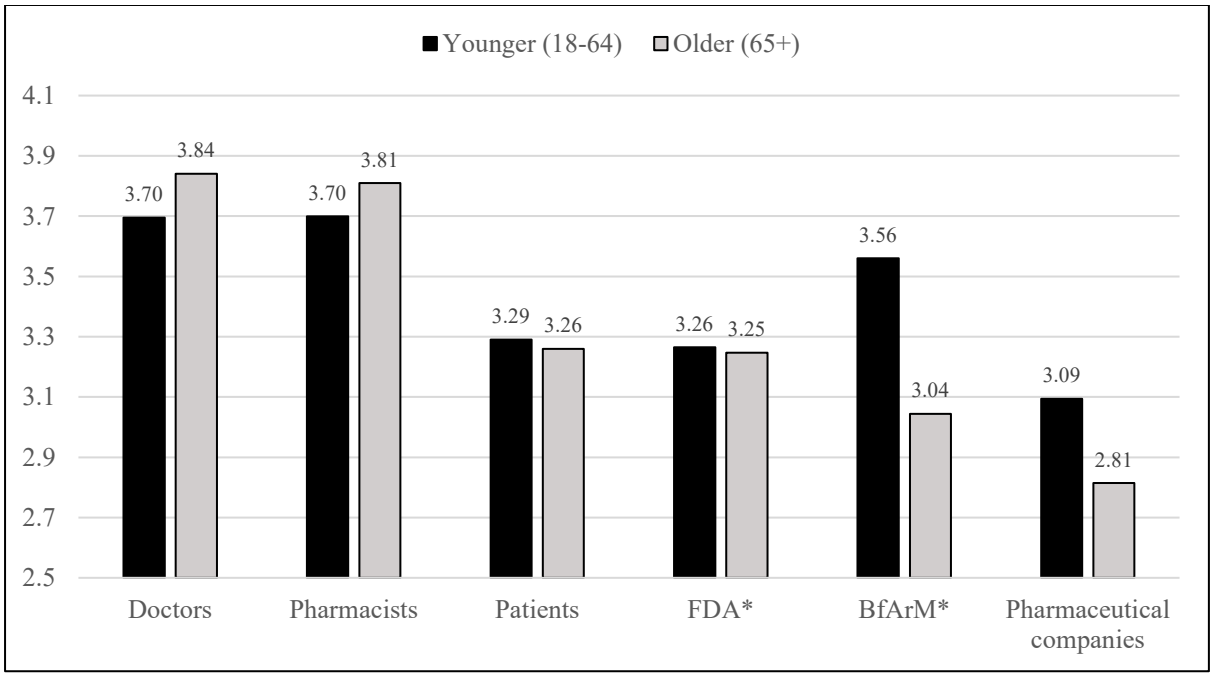

Figure 2: Older vs. younger adults' trustworthiness of 6 actors in providing medicines advice. *FDA and BfArM were only surveyed in Ohio (N=1,520) and Germany (N=1,536), respectively.

Respondents were asked to rank the five sources they rely on most for information on prescription medicines from a pre-determined list (Table 3). A total of 2,748 respondents

provided at least one rank and a total of 13,166 ranks were made. Overall, the top five most highly ranked sources were: doctors (Ranked #1), pharmacists (2), family and friends (3), specific government regulators (BfArM and FDA combined) (4), and internet search engines (5). The lowest ranked sources, that the fewest respondents selected in their top five, were Internet websites other than search engines (10), television (11), social media (e.g. Facebook, Twitter) (12), national newspapers (including their websites) (13), local newspapers (including their websites) (14), and, at the bottom of the list, the radio (15).

Notably, the rank ordering for older and younger respondents was remarkably similar (Table 3). Nevertheless, in Ohio older vs. younger adults were significantly more likely to rate doctors (29% vs. 20%) and pharmacists (25% vs. 15%) in their top three medicines information sources ($p<0.05$ on a chi-square test). Similarly, in Germany older vs. younger adults were significantly more likely to rate doctors (28% vs. 18%) and pharmacists (23% vs. 15%) in their top three ($p<0.05$ on a chi-square test) (Supplemental Table 2).

Table 3: Older vs. younger adults combined ranking of medicines information sources they rely on most.

	Younger (18-64)	Older (65+)	All
My doctor	1	1	1
My pharmacist	2	2	2
Family and friends (medically qualified or not)	3	5	3
Specific government regulators (FDA/ BfArM combined)	5	3	4
Internet search engines	4	4	5
Medical journals	6	6	6
Patient advocacy groups (including their websites)	8	7	7
Pharmaceutical companies (including their websites)	7	8	8
Pharmaceutical regulatory agencies (in general)	11	9	9
Other Internet websites	9	10	10
Television	10	11	11
Social media (e.g., Facebook, Twitter)	12	13	12
National newspapers (including their websites)	14	12	13
Local newspapers (including their websites)	13	14	14
Radio	15	15	15

(3.3) Effectiveness and side effects perceptions

Respondents were asked three related questions on their perceptions of the effectiveness and side effects of prescription medicines. First, the large majority (77%) believe that medicines work as intended for patients at least often (Table 4). In both Ohio and Germany, Older (83%) vs. younger (67%) adults were significantly more likely to perceive medicines as effective (+16% more older adults). The p-value on a chi-square test was significant at $p<0.001$ in both populations (Phi = 0.23 for Ohio and 0.25 for Germany).

Second, the majority (58%) also believe that side effects occur only occasionally, rarely, or never (Table 4). No statistically significant age differences on side effects were found.

Third, respondents were asked about 8 possible explanations for why side effects occur (Figure 3). The three most frequently perceived causes all related to patients. A large number of respondents perceived patients 'not following instructions' (54%), 'having insufficient information' (45%), and 'being unusually sensitive to the medicine' (42%) as always, very often, or often the cause. This was followed by the patient's health plan restricting access to medicines (35%) and a lack of government regulation (33%). In contrast, the majority perceived pharmacists making mistakes (89%) and doctors prescribing the wrong dosage (81%) as only occasionally, rarely, or never being the cause of side effects.

Corresponding with perceptions of key information sources (section 3.2), older vs. younger adults were significantly *less* likely to perceive doctors prescribing the wrong dosage and pharmacists making mistakes as a frequent cause of side effects ($p<0.05$ on a chi-square test) (Figure 3). In contrast, older adults were significantly more likely than their younger counterparts to attribute the causes of side effects to 'patients not following instructions'.

Table 4: Older and younger respondents' perceptions of prescription medicines' effectiveness and side effects.

	Effectiveness			Side Effects		
	Younger (%)	*Older (%)*	*All (%)*	*Younger (%)*	*Older (%)*	*All (%)*
Always	4	2	3	3	2	3
Very often	24	37	32	15	14	15
Often	39	44	42	25	25	25
Occasionally	24	13	17	39	48	45
Rarely	7	2	4	15	10	11
Never	3%	1%	2%	4%	1%	2%

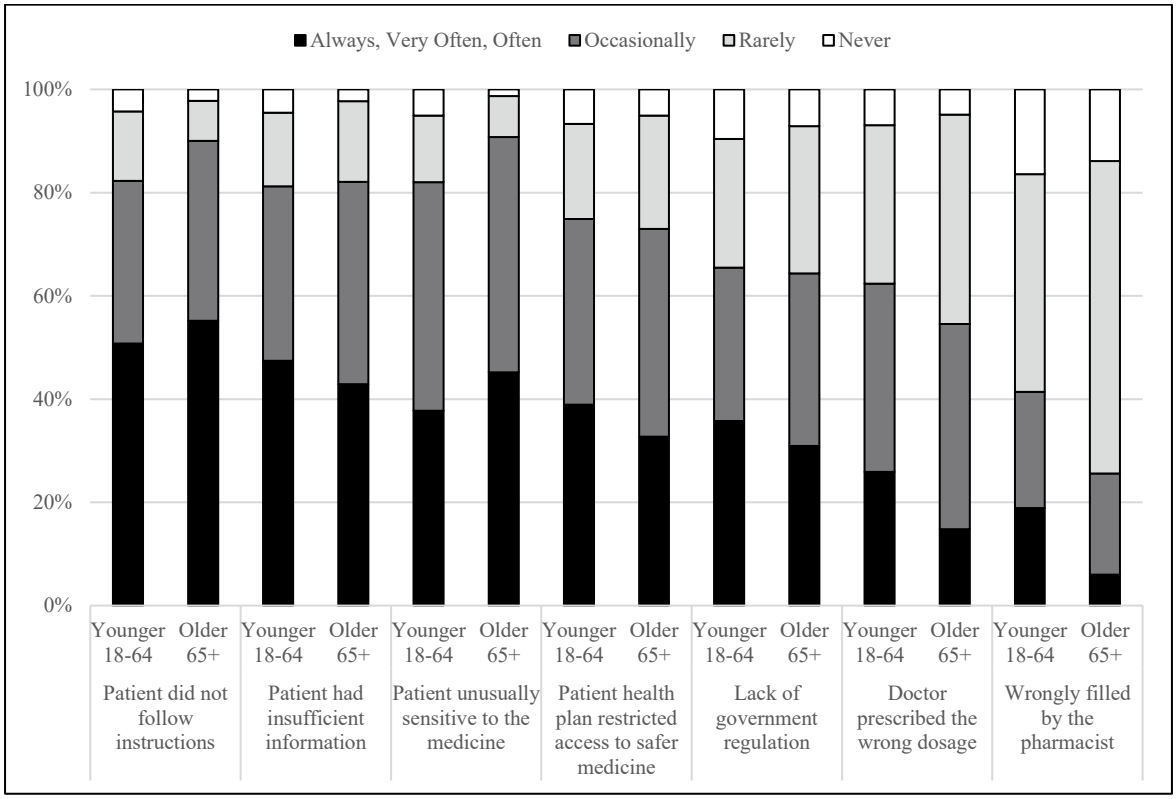

Figure 3: Bar chart showing how often older vs. younger respondents think side effects are caused by various explanations.

(3.4) Benefit-risk perceptions

The geometric mean was calculated for respondents' risk ratings for all 18 medical treatments (Supplemental Table 3). On a scale from 1 (they are not at risk) to 7 (they are very much at risk), four medical treatments with the greatest perceived risk were cancer chemotherapy (4.68), heart surgery (4.54), sleeping pills (4.25) and medicines to treat depression (4.09). Treatments with the lowest perceived risk were prostate screening tests (2.86), herbal medicines (2.65), acupuncture (2.39) and vitamin pills (2.39), which all scored a mean average of less than 3.00.

The geometric mean also was calculated for respondents benefit ratings (Supplemental Table 3). On a scale from 1 (not at all beneficial) to 7 (very beneficial), two treatments scored a mean average of over 5.00: insulin (5.11) and heart surgery (5.08). A further 11 treatments recorded a mean benefit rating of over 4.00, including: antibiotics (4.94), blood pressure medicines (4.87) and medical X-rays (4.86). Vitamin pills (3.90), acupuncture (3.84), herbal medicines (3.80), medicines to treat erectile dysfunction (3.78), and, at the very bottom of the list, sleeping pills (3.68) all received a mean average of less than 4.00.

Mean risk and benefit ratings were plotted onto a factor space (Figure 4). The plot quickly shows that perceptions of over half of all treatments surveyed (10/18) clustered together and were perceived as high benefit and low risk (top left quadrant). Three treatments were perceived as high benefit and high risk: heart surgery, cancer chemotherapy, and medicines to treat depression (top right quadrant). Acupuncture, vitamin pills, herbal medicines, and erectile dysfunction medicines were all perceived as low benefit and low risk (bottom left quadrant). Finally, sleeping pills were the only treatment considered low benefit and high risk (bottom right quadrant).

Age differences were calculated by subtracting younger adults mean risk and benefit ratings from older adults mean risk and benefit ratings, respectively. In both Ohio and Germany, older vs. younger adults perceived 7/18 treatments as significantly less risky ($p<0.05$ for chi-square test): acupuncture (-0.49), flu vaccine (-0.35), blood pressure medicines (-0.25), vitamin pills (-0.24), prostate screening tests (-0.23), MMR vaccine (-0.19), and insulin (-0.12). This was the only direction in which a significant relationship was found for respondents' risk perceptions.

In both Ohio and Germany, older vs. younger adults also perceived 8/18 treatments as significantly more beneficial (chi-square p-value < 0.05): flu vaccine (+0.75), heart surgery (+0.67), insulin (+0.64), antibiotics (+0.64), blood pressure medicines (+0.60), medical X-rays (+0.40), medicines for cholesterol (+0.39), and the MMR vaccine (+0.34). Again, in both Ohio and Germany this was the only direction in which a significant relationship was found for respondents' benefit perceptions.

Medical treatments with a combined benefit and risk age difference of more than 0.50 were plotted onto a second factor space (Figure 5). These were the flu vaccine (1.09), blood pressure medicines (0.85), insulin (0.76), heart surgery (0.75), antibiotics (0.70), acupuncture (0.66), the MRR vaccine (0.53), and prostate screening tests (0.52). Notably, older vs. younger adults perceived all but three of these treatments – heart surgery, antibiotics, and acupuncture –as both significantly less risky and significantly more beneficial.

(3.5) Affect and benefit-risk perceptions

Correlations between respondents' positive/ negative affect scores (section 3.1) and risk and benefit perceptions (section 3.5) were examined for all 18 medical treatments (Supplemental Table 4). First, there was a greater correlation between older vs. younger adults' risk perceptions and positive/negative affect in both Ohio and Germany for 10/18 treatments: medicines for erectile dysfunction, antibiotics, sleeping pills, herbal medicines, medicines for cholesterol, blood pressure medicines, flu vaccine, allergy medicines, prostate screening tests, and acupuncture (Supplemental Table 4). For the other eight medical treatments, there is no case in which *both* the Ohio and German samples show affect as more important for risk perceptions in the younger sample. The reason is that for these eight medical treatments, we see mixed effects (e.g., for vitamin pills, younger adults in Ohio have a stronger relationship between affect and risk perceptions than older adults in Ohio do, but the relationship is reversed in Germany). Second, there was also a greater correlation between older vs. younger adults' benefit perceptions and positive/ negative affect scores in both Ohio and Germany for 16/18 medical treatments (Supplemental Table 4). Medical x-rays and acupuncture were the only two medical treatments for which this was not true. Taken together, older vs. younger adults were found to rely more on positive/ negative affect to inform their benefit and risk perceptions for most medical treatments surveyed.

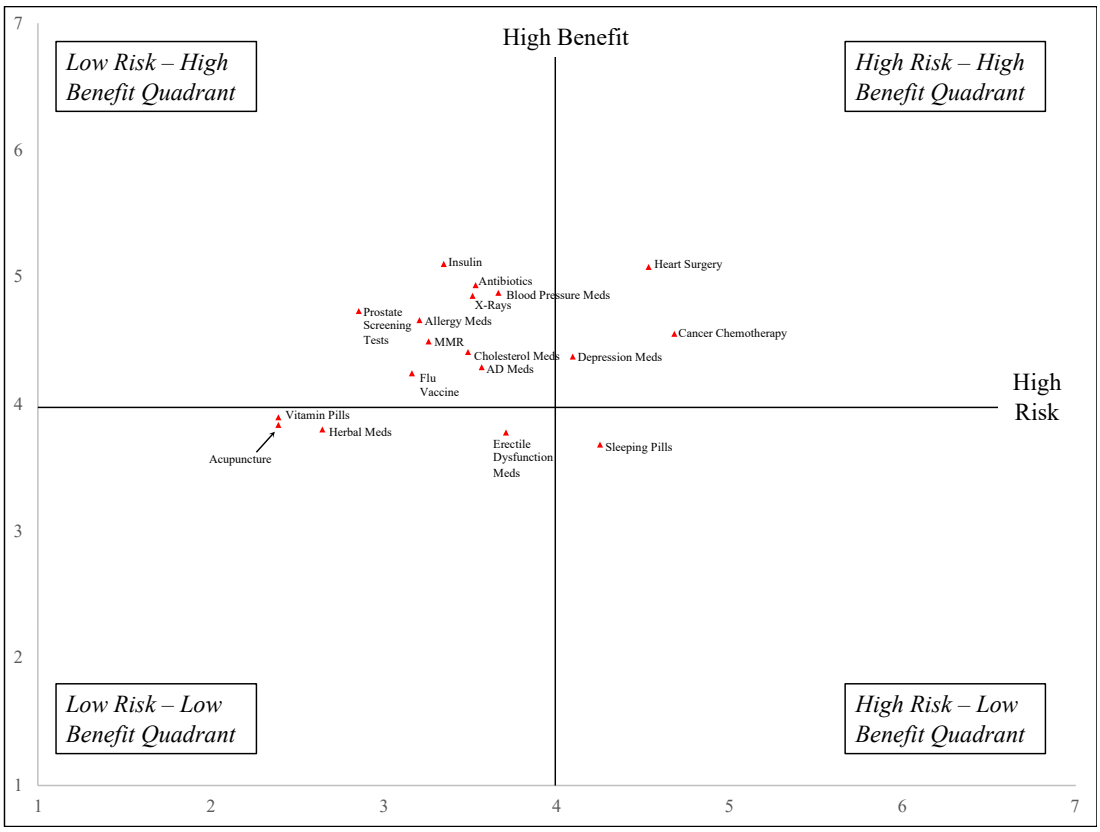

Figure 4: Respondents' benefit-risk ratings for 18 medical treatments. MMR = Mumps Measles and Rubella Vaccine; AD = Medicines to treat Alzheimer's Disease

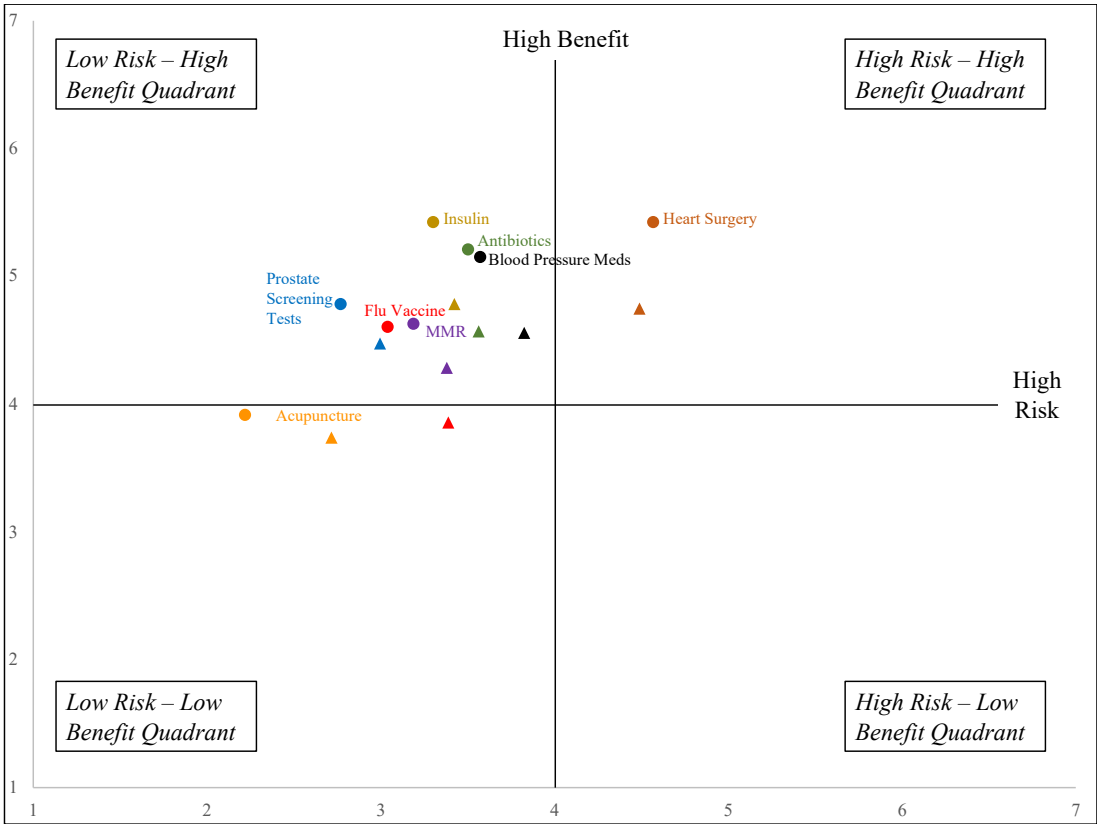

Figure 5: Older and younger respondents' combined benefit and risk ratings for 8 medical treatments that had a 0.50 or larger combined benefit-risk perception age difference. Circle = Older respondents; Triangles = Younger Respondents.

(4.) Discussion

This study investigated age differences in adults' pharmaceutical benefit-risk perceptions. By conducting a representative survey in the USA and Germany, the results show clear and significant differences between adults aged 18-64 years old (younger group) and those aged 65 years and older (older group), which strongly supports recent pilot findings [15].

(4.1) Benefits and effectiveness perceptions

The cross-sectional survey revealed that older adults from the USA and Germany perceive prescription medicines – including their benefits and effectiveness – significantly more positively than their younger counterparts. Older adults were significantly more likely to (1) associate prescription medicines to positive mental representations (section 3.1), and (2) perceive that medicines work as intended at least often (section 3.3). Older adults also were significantly likely to perceive 8/18 *specific* medical treatments as more beneficial, with all 10 other items surveyed having no observed benefit perception age differences (section 3.4).

One reason for these clear age differences may well be that adults from the USA and Germany aged 65 years and over (older group) consume considerably more medicines than those aged 18-64 years (younger group) [25, 26, 39]. Martin *et al*. [25] found that 85% of US adults aged 60 years and older used at least one prescription medicine over a 30-day period in 2015-2016, compared to 47% aged 20-59 years old. Similarly, 86% of adults aged 65 years and older in Germany self-reported using at least one prescription medicine over a two-week

period in 2014[5], compared to 43% aged 15-64 years old [26]. Greater use means that older adults gain more therapeutically, which is likely to contribute to their more positive prescription medicines' perceptions for relevant treatments. For example, the five survey items with the largest benefit perception age differences – the flu vaccine, heart surgery, insulin, antibiotics, and blood pressure medicines – are all more beneficial for older adults at the population level. While older adults are at higher risk of influenza complications [40], they also have a higher prevalence of heart disease, high blood pressure, and diabetes [24, 41-42]. In contrast, no significant benefit perception age differences were found for herbal medicines, acupuncture, vitamin pills, medical X-rays, or allergy medicines, all of which arguably have similar benefits for adults of all ages.

(4.2) Risk perceptions

In comparison with respondents' benefit perceptions (section 4.1), the survey revealed that older adults had significantly lower risk perceptions for 7/18 treatments, with no significant age differences identified for all 11 other items. Interestingly, only 4 of these treatments – flu vaccine, blood pressure medicines, insulin, and the MMR vaccine – were perceived as both significantly less risky and more beneficial by older adults. This suggests that, although perceived benefit and perceived risk are inversely related [3], age influences benefit and risk judgements differently [15].

The results also compare well with several past studies that found older adults perceive lower risk for a wide variety of hazards and technologies [16, 43-44], including medical treatments [15]. Yet, significant risk perception age differences were not found for all items surveyed (section 3.4). Older versus younger adults therefore do not necessarily perceive greater or less risk *in general*. Indeed, other studies show that older adults perceive significantly *greater* risk for various technological, social, and natural hazards [45-47]. Further, Hanoch *et al.* [23] conducted a cross-sectional study with 317 adults aged 20-77 and found no significant age differences in medical risk-taking tendencies. This variety of findings provide strong evidence that age-related influences on risk perceptions vary depending on several currently unexamined contextual factors such as risk domain or type of hazard [23]. The present study goes further by finding that, even within the medical domain, the risks of various treatments are perceived differently by older and younger adults. As more evidence accumulates, a fruitful new line of inquiry would be to investigate these contextual factors more comprehensively and better understand under what conditions and for which hazards/ technologies/ medical treatments older versus younger adults perceive greater or less risk [15].

(4.2) Reliance on the affect heuristic

When combining older and younger adults' benefit and risk perceptions, a remarkably familiar pattern was found (Figure 4). Most medical treatments (10/18) were perceived as low risk and high benefit. A second group – vitamin pills, herbal medicines, acupuncture, and erectile dysfunction medicines – were also perceived as low risk but with distinctly lower benefits. Three other items – heart surgery, cancer chemotherapy, and medicines for depression – were perceived as high risk and high benefit. Finally, only one item – sleeping pills – was perceived as both high risk and low benefit. These groupings are highly consistent with comparable survey research conducted in Canada, Sweden, the USA, and Ireland [1-3,

[5] Data for the year 2019 are expected in mid-2020.

15]. In particular, respondents had remarkably similar benefit-risk perceptions for almost all medical treatments surveyed in both the present study and Slovic *et al.*'s [3] 2007 study of US adults (N=2,071). One particularly notable exception, however; was the marked reduction between 2007 and 2018 of perceived benefit for vitamin pills, the flu vaccine, and the MMR vaccine (*see* [3] p95). Although Slovic *et al*. [3] specified 'vaccines' more generally than 'the flu vaccine' or 'the MMR vaccine', research shows that adults' acceptance of vaccines has wavered in the USA and Europe [48-49].

Moreover, older adults' benefit-risk perceptions were found to be more greatly correlated with measures of affect (section 3.5). Specifically, for most medical treatments, a greater correlation was found between older adults' affective imagery and both their risk perceptions and benefit perceptions. In this context, the affect heuristic refers to patients' reliance on the specific feelings of "goodness" or "badness" they associate with a given medical treatment [36, 50-51]. An array of past studies has demonstrated that perceived risk and perceived benefit of an activity (e.g. medicines taking) are linked to the strength of the positive or negative affect associated with that activity [50-54]. Affect guides benefit-risk perceptions with more positive affect associated with lower risks and higher benefits and, inversely, more negative affect associated with higher risk and lower benefit [36]. Crucially, recent judgement and decision-making research demonstrates that adults rely more on positive/ negative affect as they age [32, 38]. The present study therefore strongly supports these findings by showing that older adults rely more on positive/ negative affect when forming their benefit-risk perceptions [cf. 33]. It was particularly striking to find that older adults' positive/ negative affect scores were significantly more correlated to perceived benefit for 16/18 medical treatments, i.e. all but two items (section 3.5).

(4.3) Trust in doctors and pharmacists

This study supports growing evidence that older versus younger adults are consistently more positive about prescribing doctors and pharmacists [15, 55-56]. Older adults were found to be significantly more likely to rate prescribing doctors and pharmacists highly, perceive them as more trustworthy, and rely on them as sources of prescription medicines information (section 3.2). Although younger adults still rated doctors and pharmacists favorably, there is now clear evidence that older adults are much more positive about these two key medical actors.

Age differences in the information sources patients trust, rate as competent, and rely on is fundamentally important for ensuring the safe and effective use of medicines [6, 57]. High trust contributes towards patient satisfaction, adherence to treatment, and improved health outcomes [58-60]. For example, a large cross-sectional survey [9] conducted in 6 European countries (N=6,001) found strong associations between patients' perceived trustworthiness of medical actors, such as doctors and pharmacists, and their behavioral intentions. Higher trust in medical sources such as doctors and pharmacists were particularly strongly associated with patients adopting recommended medicine-taking behavior and seeking more information if they believed something was wrong with their medicine [9]. If, as this study shows, older adults perceive doctors and pharmacists as more trustworthy, then one would expect older adults to adopt more positive medicine-related behavior. Younger adults would, inversely, be expected to adopt less positive behavior. This raises important unanswered questions about why these age differences exist. Will younger adults perceive their doctors and pharmacists as more trustworthy as they grow older, or do these findings signal ingrained and enduring

inter-generational differences between today's older and younger generations? Answering these questions call for future longitudinal studies.

(4.4) Notable similarities

While the main aim of this study was to identify age differences, the results also revealed at least two notable *similarities*. One is that adults of all ages *relied* on very similar sources of prescription medicines information (section 3.2). While doctors and pharmacists topped the rankings, sources such as social media, newspapers, and the radio ranked the lowest. One implication is that, although older adults perceive doctors and pharmacists as more trustworthy and rate them more highly (section 4.3), adults of all ages in the USA and Germany still rely on them the most [6, 9]. A second implication is that, perhaps surprisingly, adults of all ages have a comparably low reliance on social media, local and national newspapers, and the radio, which have starkly different uptakes by different generations. It is well-known that older adults are more likely to listen to the radio and buy broadsheet newspapers, and less likely to use the Internet, own a smartphone, and use social media [61-64]. For example, Anderson and Perrin [63] found that in 2016 only 34% of US adults aged 65 years and over ever use social networking sites such as Facebook or Twitter compared to 69% aged 18 years and older, even though social media use has substantially increased in older US populations over the past 15 years. The results therefore demonstrate a crucial difference between (1) the sources that adults rely on most when *seeking* prescription medicines information (i.e. doctors, pharmacists) and (2) the varying channels they use to consume information in general– whether they receive medicines-related information or not (e.g. social media, the radio, newspapers) [65-67].

A second notable similarity was that adults of all ages are more likely to attribute the causes of side effects to patients than any other actor surveyed (section 3.2). This includes patients not following instructions, having insufficient information, and being unusually sensitive to medicines (Figure 3). Slovic *et al*. [3] and Balog-Way and Löfstedt [15] both reported similar findings. These findings together suggest that respondents' perceptions of side effects are highly susceptible to fundamental attribution bias, "the tendency to overestimate the degree to which an individual's behavior is determined by his or her abiding personal characteristics, attitudes, or beliefs and, correspondingly, to minimize the influence of the surrounding situation on that behavior" [68]. Adults of all ages tended to attribute the causes of side effects more to patients and less to other situational factors such as the role of governments, the healthcare system, doctors, and pharmacists. Individualistic Western cultures (e.g. the USA and Germany) compared to collectivistic East Asian cultures (e.g. Japan, Korea, China) also tend to focus their attributions more on the individual person [69-70], although *see* [71]. Future research therefore should investigate whether adults from collectivistic countries attribute the causes of side effects less to patients and more to the situation surrounding patients (e.g. healthcare system, or prescribing doctor) compared to patients from Western countries.

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Supplemental material

Supplemental Table 1: Respondents' sex, age, job status and educational attainment.

		Ohio	Germany
Sex (%)	Male	47	50
	Female	52	50
	Other / prefer not to say	1	0
Age (%)	18-64	66	67
	65+	34	33
Job status (%)	Working full time	28	35
	Working part time	12	13
	Retired	34	38
	Unemployed (looking for work)	8	4
	Full-time Homemaker with no outside employment	10	6
	Student	3	3

	Other	6	3
Ohio Education (%)	Some schooling completed / No high school diploma	7	-
	High school graduate or equivalent	35	-
	Some college / no degree	22	-
	Associate degree	8	-
	Bachelor's degree	18	-
	Graduate or professional degree	10	-
Germany Education (%)	No schooling or vocational training	-	1
	Secondary school without completed vocational training (POS 8 classes)	-	5
	Secondary school with completed vocational training (POS 8 classes)	-	12
	Middle school, secondary school without Abitur (POS 10 classes)	-	39
	Abitur, university entrance qualification (EOS, 12 classes)	-	18
	University, technical college, polytechnic, technical college	-	24
	Scientific doctorate	-	2

Supplemental Table 2: Relative frequency with which a source was listed as one of a respondent's top three sources they relied on for medicines information.

	Ohio		**Germany**	
	Younger (%)	Older (%)	Younger (%)	Older (%)
Doctors	65.9	84.6	62.4	84.1
Pharmacists	50.2	72.9	52.9	69.5
Family and friends	31.2	20.5	37.5	22.7
Internet search engines	30.3	27.6	26.3	14.9
FDA / BfArM	25.9	21.5	25	21.3
Medical journals	19	10.6	21.5	23
Pharma. companies	18.6	11.1	16.8	11.6
Patient advocacy groups	16.2	8.7	18.3	18.1
Social media	15.7	3.6	14.4	4.8
Television	15.1	7	16.9	7.6
Other Internet websites	14.5	9.2	17.8	6.2
Radio	11.7	3.6	12.8	4.2
National newspapers	11.4	2.5	10.9	5.7
Local newspapers	10.7	3.5	13.7	4.9

Supplemental Table 3. Mean risk and benefit perception

	RISK PERCEPTIONS			BENEFIT PERCEPTIONS		
	Younger	*Older*	*All*	*Younger*	*Older*	*All*
Medicine to treat depression	4.06	4.11	4.09	4.20	4.45	4.37
Medicines to slow the progression of Alzheimer's disease	3.61	3.54	3.56	4.16	4.37	4.29
Medicines to treat erectile dysfunction (e.g. Viagra)	3.62	3.76	3.71	3.75	3.80	3.78
Antibiotics	3.57	3.51	3.53	4.57	5.20	4.94
Sleeping pills	4.08	4.37	4.25	3.77	3.63	3.68
Herbal medicines	2.67	2.64	2.65	3.80	3.79	3.80

Cancer chemotherapy	4.62	4.75	4.68	4.39	4.67	4.56
Insulin	3.43	3.31	3.35	4.78	5.42	5.11
Medicines for cholesterol (e.g. statins)	3.54	3.45	3.48	4.16	4.55	4.42
Vitamin pills	2.55	2.30	2.39	3.96	3.87	3.90
Blood pressure medicines	3.83	3.57	3.66	4.55	5.14	4.87
MMR vaccine	3.38	3.19	3.26	4.28	4.62	4.50
Flu vaccine	3.39	3.04	3.17	3.86	4.60	4.24
Allergy medicines	3.20	3.21	3.21	4.49	4.74	4.66
Heart surgery	4.50	4.57	4.54	4.74	5.41	5.08
Medical x-rays	3.57	3.49	3.52	4.54	4.94	4.86
Prostate screening tests	3.00	2.77	2.86	4.47	4.77	4.73
Acupuncture	2.72	2.22	2.39	3.74	3.91	3.84

Supplemental Table 4: Correlations between valence of word associations with 18 medical treatments and corresponding perceptions of (1) risk and (2) benefit.

	RISK PERCEPTIONS				BENEFIT PERCEPTIONS			
	Ohio		**Germany**		**Ohio**		**Germany**	
	Younger	*Older*	*Younger*	*Older*	*Younger*	*Older*	*Younger*	*Older*
Medicines for depression	-0.18	-0.29	-0.14	-0.13	0.42	0.51	0.34	0.52
Medicines for Alzheimer's disease	-0.10	-0.15	-0.13	-0.09	0.41	0.50	0.24	0.44
Medicines for erectile dysfunction (e.g. Viagra)	0.00	-0.27	-0.16	-0.25	0.40	0.48	0.28	0.46
Antibiotics	-0.21	-0.24	-0.05	-0.16	0.39	0.44	0.33	0.44
Sleeping pills	-0.23	-0.26	-0.06	-0.17	0.41	0.44	0.25	0.38
Herbal medicines	-0.09	-0.23	-0.11	-0.23	0.45	0.53	0.41	0.46
Cancer chemotherapy	-0.08	-0.28	-0.18	-0.16	0.28	0.44	0.26	0.33
Insulin	-0.12	-0.21	-0.12	-0.11	0.35	0.37	0.32	0.45
Medicines for cholesterol (e.g. statins)	-0.21	-0.39	-0.06	-0.17	0.39	0.55	0.27	0.43
Vitamin pills	-0.19	-0.17	0.00	-0.15	0.42	0.51	0.36	0.48
Blood pressure medicines	-0.17	-0.30	-0.08	-0.14	0.36	0.47	0.31	0.48
MMR vaccine	-0.30	-0.40	-0.22	-0.16	0.50	0.55	0.37	0.42
Influenza vaccine	-0.29	-0.47	-0.27	-0.39	0.51	0.65	0.31	0.55
Allergy medicines	-0.13	-0.22	-0.05	-0.15	0.35	0.44	0.29	0.40
Heart surgery	-0.11	-0.11	-0.06	0.01	0.25	0.26	0.12	0.32
Medical x-rays	-0.13	-0.24	-0.20	-0.17	0.40	0.38	0.23	0.40

Prostate screening tests	-0.15	-0.29	-0.14	-0.25	0.33	0.47	0.26	0.45
Acupuncture	-0.07	-0.19	-0.12	-0.21	0.44	0.56	0.46	0.45

*For risk perceptions, a negative value for a correlation indicates that a more positive word association is associated with belief that the treatment poses less risk. For benefit perceptions, a positive value for a correlation indicates that a more positive word association is associated with the treatment being more beneficial.